extruded from regenerated mulberry, wild or spider silk or fibres extruded from a recombinant protein based on the proteins of mulberry silk, wild silk or spider silk or a combination of these.

[0066] The silk fibre lay consists of strands of degummed or raw silk consisting of six to nine silk baves lightly twisted round each other. Alternatively, the silk fibre lay may be formed from silk sliver fibres, from silk thread formed by twisting silk sliver fibres, from silk monofilaments, from silk monofilaments twisted together, from undegummed silk baves, from degummed silk brins, from threads formed from two to eight former strands twisted together or from silk threads plaited or braided together.

[0067] The hydrogel has an open pore structure and consists of native or regenerated silk fibroin from mulberry, wild or spider silk. Alternatively the hydrogel may consist of gelatin, fibrin, fibronectin, alginate, hyaluronic acid, chondroitin sulphate or a combination of these.

[0068] Where the porous hydrogel is proteinaceous it can be cross-linked by immersion in a covalent cross-linking agent.

[0069] Where the porous hydrogel is comprised of fibroin it can be cross-linked by hydrogen bonds by treatment with 30-70% ethanol.

[0070] Either form of cross-linking influences the mechanical properties and resorption time of the both the hydrogel and the silk fibre lay. A range of different cross-linking agents may be used to cross-link hydrogels of different compositions. For example these include: members of the aliphatic aldehyde series, dialdehydes, carbodiimides, succinimides, succinamides, peroxidases in the presence of hydrogen peroxide, transglutaminases, phenoloxidases, phenolases, tyrosinases and/or Fenton reaction catalysts.

[0071] The resorption time can also be tuned by varying the hydrophobicity of the protein or proteins by alkylating with hydrophobic side chains. Hydrophilic carboxyl, hydroxyl, amine and sulphydryl side chains of amino acids within silk proteins may be used as sites for such acylation. Alternatively, a wide range of monofunctional, bifunctional or polyfunctional acylating agents may be used to increase the hydrophobicity of proteins. In the case of bi- or polyfunctional acylating agents these have the additional effect of cross-linking the protein components. Acylating agents that can be used to increase the hydrophobicity of the proteins include, for example, arylating and alkylating agents. Further acylating agents suitable for increasing the hydrophobicity of the proteins include perfluorobutanoyl chloride, lauroyl chloride, myristoyl chloride, benzophenonetetracarboxylic acid, diaminodiphenyloxide, aliphatic and bifunctional isocyanates, dodecyl ioscyanate, hexamethylene diisocyanate, aliphatic anhydrides and octadecenyl succinic anhydride.

[0072] One or more growth factors are incorporated in or covalently bound to the hydrogel of the body of the device (**2**, **6**). These growth factors stimulate the binding and/or differentiation of mesenchymal or stem cells to either form cartilage or to secrete protoglycan. Suitable growth factors include Beta-FGF, TGF-beta 1, GDF-5, insulin-like growth factor, basic fibroblast growth factor, cartilage tissue growth factor or osteogenic protein-1. One or more synthetic drugs with analogous functionality to the growth factors may be used to replace or augment the functionality of the natural growth factors.

[0073] Similarly one or more covalently bound growth factors are incorporated into the marginal flanges or extensions of the device (**1**, **4**). These growth factors stimulate the recruitment, binding and/or differentiation of mesenchymal or stem cells to secrete normal bone. Suitable growth factors include a bone morphogenetic protein, a TGF-beta, an epidermal growth factor, an insulin-like growth factor, growth/differentiation factor-10 or Runx2 (Cbfa1/AML3) transcription factor. One or more covalently bound synthetic drugs with analogous functionality to the growth factors may be used to replace or augment the natural growth factors.

[0074] Living cells may be incorporated directly into a solution of ungelled fibroin and alginate monomers made up in modified cell culture media. The resulting cell suspension is then incorporated into the device either before completing the laying down of the fibre lay or into preformed hydrogel scaffolds. After incorporation, the alginate monomers are caused to polymerise. Living cell suspensions may be mixed with alginate solutions made up in low calcium cell culture medium. Such a mixture may subsequently be gelled by the addition of a cell-compatible concentration of calcium.

[0075] Similarly, regenerated silk fibroin solutions remain a sol in neutral or slightly alkaline cell culture medium but slowly form a gel when slightly acidified with phosphate buffer. This enables living cells to be incorporated into porous fibroin hydrogels.

[0076] FIGS. **3** and **4** show a schematic representation of an embodiment of an intervertebral disc repair device according to the invention.

[0077] In this embodiment there is a cylindrical nucleus pulposa analogue (**15**) of regenerated silk fibroin hydrogel combined with randomly oriented silk fibres (not shown). This nucleus pulposa analogue (**15**) forms the core around which an annulus fibrosa analogue (**14**) is laid. The annulus fibrosa analogue (**14**) consists of silk fibres laid down around the nucleus pulposa analogue (**15**) in a trellis-like arrangement. Premineralised sheets of fibrelay and hydrogel (**13**, **16**) are incorporated into the device as successive layers of the annulus fibrosa analogue (**14**) are laid down. The premineralised sheets (**13**, **16**) form the top and bottom of the device and facilitate the integration of the device with the bony surface of the vertebral centrum of a patient. The premineralised sheets (**13**, **16**) are extended laterally beyond the annulus fibrosa analogue (**14**) in order to facilitate anchoring of the device to the bony surfaces of the vertebral centra.

[0078] The three-dimensional fibre lay consists of layers of radially oriented silk fibres at the top and bottom of the device (**9**) together with silk fibres laid down in successive concentric cylindrical layers (**10**). A porous regenerated silk fibroin hydrogel (**11**) holds the fibres and layers of fibres together. The fibres in any particular cylindrical layer are laid down parallel to one another and are tilted at a constant angle to the vertical axis of the device (**12**). The tilt of the fibres alternates to left and right in successive cylindrical layers to form a trellis-like structure (**12**).

[0079] The anatomically-shaped intervertebral disc repair device closely resembles the meniscal repair device described above other than in the nature of the fibre lay.

[0080] The fibre lay of the intervertebral disc repair device also uses a combination of winding and stitching, though can alternatively be produced by weaving, twisting, braiding, knitting, or embroidery or a combination of these.

[0081] The fibre lay of the intervertebral repair device basically has three components: a nucleus pulposa analogue (**15**),